989-59 Platelet-Leukocyte Interaction in Patients with Unstable Angina

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Experimental studies show an increased interaction between endothelial cells, leukocytes and platelets in ischemia, which is associated with a release of mediators that cause microvascular damage. Aim of the study was to investigate the platelet-leukocyte interaction in patients with unstable angina and its effect on neutrophil function. Systemic venous blood samples were taken from 20 patients with stable and from 20 patients with unstable angina pectoris, as well as from 20 healthy controls. After incubation with FITC-labelled mAbGPIIb-IIIa mean cellular fluorescence of neutrophils (PMN) and monocytes (Mo), identified by CD45 or CD14 binding, was analysed by flow cytometry. Patients with unstable angina showed a significant increase in platelet-neutrophil and platelet-monocytes conjugates.

	Unstable	Stable angina	Controls
GPIIbIIIa-Mo	200 ± 37+,*	95 ± 15	72 ± 11
GPIIbIIIa-PMN	132 ± 20.5+,*	29.5 ± 4.7	19.1 ± 4.1

+p < 0.05 vs. stable angina, *p < 0.05 vs. controls

As evidence of systemic neutrophil activation, an increased surface CD11b expression and a shedding of LECAM-1 on circulating neutrophils was found in unstable angina compared to stable angina (mean fluorescence CD11b: 115.6 ± 10.3 vs. 74.0 ± 6.3, p = 0.002, mean fluorescence LECAM-1: 49.8 ± 6.0 vs. 72.1 ± 4.0, p = 0.06), which could be related to the extent of platelet-neutrophil interaction (CD11b: r = 0.5, p = 0.0005; LECAM-1: r = 0.42, p = 0.012). In vitro studies revealed that binding of purified platelet membranes to separated neutrophils caused a dose dependent increase in CD11b surface expression and shedding of surface LECAM-1. Thus, the study demonstrates that the increased interaction between platelets and leukocytes contributes to the leukocyte activation in unstable angina.

989-60 Site of Leukocyte Activation in Unstable Angina

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Recent research suggests that inflammatory indexes are increased in unstable angina; however it is not known if they reflect inflammatory activity in the coronary arteries or the effects of recurrent ischemia on the myocardium. To address this issue, in 20 pts with unstable angina (defined as recurrent chest pain at rest associated with transient ST-T changes) blood samples were simultaneously taken from the coronary sinus (CS), from aorta (Ao) and from the coronary artery (CA) just distally to the culprit lesion. Surface expression of neutrophils (PMN) and monocytes (MONO) CD11B/CD18 adhesion receptors was detected by direct immunofluorescence evaluated by flow cytofluorimetry using monoclonal antibodies tagged with fluorescent markers. Results are given as molecular equivalents of soluble fluorescein.

	Ao	CA	CS
PMN	28.5 ± 4.1	23.1 ± 3.2	37.3 ± 5.1 *,†
MONO	23.7 ± 3.9	27.6 ± 4.6	33.1 ± 4.8§

*p < 0.02 CS vs Ao, †P < 0.0.2 CS vs CA, §p < 0.02 CS vs AO

These data show that in patients with unstable angina a significant upregulation of CD11B/CD18 adhesion receptors of neutrophils and monocytes occurs in the coronary sinus as compared to the aorta and the culprit lesion site suggesting that leukocyte activation takes place at the microcirculatory level and not within the epicardial coronary arteries.

990 Clinical Aspects of Myocardial Ischemia: Silent Ischemia, Pre-PTU Medical Therapy, and Risk Stratification

Wednesday, March 22, 1995, 9:00 a.m.–11:00 a.m. Ernest N. Morial Convention Center, Hall E Presentation Hour: 10:00 a.m.–11:00 a.m.

990-46 Decreased Heart Rate Variability Precedes Daily Life Ischemia

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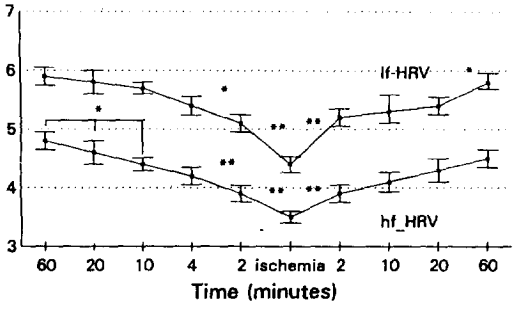
Triggers of daily life ischemia remain undefined. Evidence suggests that vagal withdrawal may produce ischemia by coronary vasoconstriction. Heart rate variability (HRV) has been shown to be an indicator of vagal tone. Therefore, we analyzed 68 asymptomatic ambulatory ischemic events (>1 mm downsloping ST depression, for >60 sec) in 19 men with documented coronary disease during 48 h Holter monitoring. HRV was examined using spectral analysis distinguishing low frequency (lf = 0.04–0.15 Hz) and high frequency (hf = 0.15–0.40 Hz) HRV at 60-, 20-, 10-, 4-, and 2-minutes prior to, and 2-, 10-, 20-, and 60-minutes after ischemia. To control for heart rate, HRV was also assessed at similar heart rates during non-ischemic periods. A significant ($p < 0.05$) decrease in hf-HRV was observed in the 10–60 min periods prior to ischemia and a further drop emerged at both 4- and 2-min prior to ischemia. In addition, hf-HRV was significantly lower 10- and 4-min prior to ischemia (4.26 ± 0.13 and 4.22 ± 0.15) than in the heart rate controlled periods (4.96 ± 0.29 and 4.93 ± 0.26). Results for lf-HRV were similar.



Conclusion: Decreased HRV precedes ischemia and suggests the possibility of vagal withdrawal as a trigger of daily life ischemia.

990-47 Absence of Ischemia on Ambulatory ECG Monitoring During Treatment as a Predictor of Outcome: A Report from the ACIP Study

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The presence of ischemia on ambulatory ECG (AECG) monitoring adversely influences the outcome in patients with coronary artery disease. In the Asymptomatic Cardiac Ischemia Pilot (ACIP), 618 clinically stable patients with revascularizable coronary artery disease, abnormal stress tests and asymptomatic ischemia on AECG monitoring were randomized to 1 of 3 treatment strategies: angina-guided care, ischemia-guided care or revascularization. Repeat AECG monitoring was done at 12 weeks on treatment and the patients were followed for outcome analysis at 1 year.

At 1 year death, MI or hospitalization occurred in 38 of 262 patients without AECG ischemia at 12 weeks (14.5%), and 55 of 272 (20.2%) of those with AECG ischemia at 12 weeks ($p < 0.08$). Aggregate adverse outcomes (death, MI, hospitalization or ischemia on 1 year ETT) occurred in 160 (61%) of patients without AECG ischemia at 12 weeks and 225 (83%) of patients with AECG ischemia at 12 weeks ($p < 0.001$).

These data provide evidence to support the hypothesis that AECG monitoring results during treatment may be predictive of future coronary events.

990-48 Additive Effect of Exogenous and Endogenous Factors in the Circadian Variation of Ambulant Myocardial Ischemia

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The circadian rhythm of myocardial ischemia is well-established, with a peak occurring between 6 a.m. and noon. This circadian rhythm has been related to diurnal variations in exogenous triggers of ischemia (physical and mental activities). To determine if an underlying endogenous circadian vulnerability for ischemia exists independently of the 24-hour changes in exogenous triggers, we analyzed data of 63 patients (mean age 62 ± 8 years) with documented coronary artery disease with >24 hr Holter monitoring for ischemia (≥1 mm horizontal or downsloping ST depression, or ≥1.5 mm upsloping, for <1 min). A validated structured diary system was used to assess physical and mental activities throughout the day. To assess the endogenous component, diurnal fluctuations of ischemia were analyzed while statistically controlling for concomitant changes in physical and mental activity using residualized regression scores. The morning increase in ischemia co-occurred with increases in both physical and mental activity. During the morning, 77% of the ischemic periods occurred at high physical activity, while activity was high in 48% of the non-ischemic morning-observations ($p < 0.05$). For mental activity these percentages were 45% and 29% ($p < 0.05$). Exogenous factors affected onset of ischemia to a lesser extent in the afternoon and